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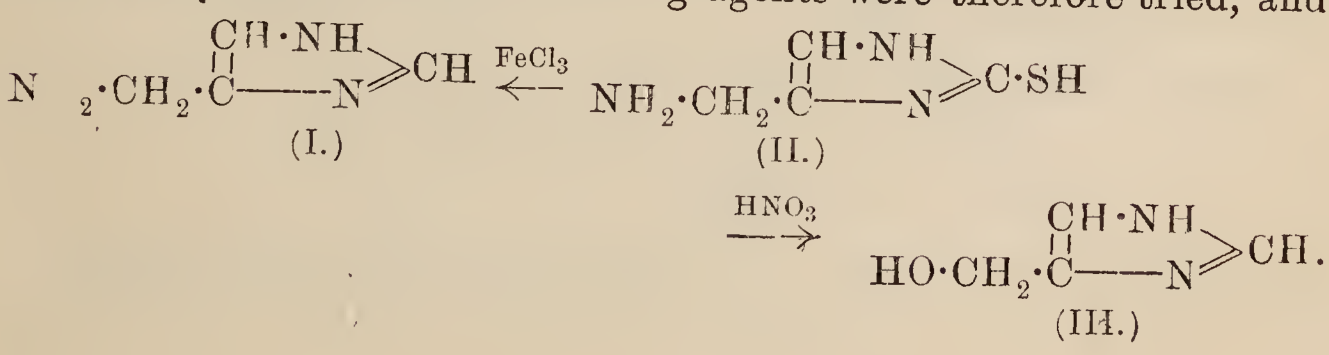
CCXLV.—*Aminoalkylglyoxalines.*

By Frank Lee Pyman.

In view of the great physiological activity of 4(or 5)-β-aminoethylglyoxaline (compare Dale and Laidlaw, *J. Physiol.*, 1910, **41**, 318), the preparation of several of its homologues has been carried out, and these have been physiologically tested by Dr. P. P. Laidlaw, of the Wellcome Physiological Research Laboratories, to whom the author is indebted for the results given in this paper. In this connexion the recent preparation of other homologues of this base by Ewins (this vol., p. 2052) may be noted.

Barger and Dale (*J. Physiol.*, 1910, **41**, 19), in dealing with the relationship between the chemical constitution of the amines and their physiological action, have shown that the activity varies greatly with the length of the side-chain; in the fatty series the maximum of activity is attained at hexylamine, whilst the most active phenylalkylamine is phenylethylamine, having a fatty side-chain of two carbon atoms. It appeared, therefore, of interest to determine the optimum length of side-chain for physiological effect in the aminoalkylglyoxalines. For comparison with 4(or 5)-β-aminoethylglyoxaline, 4(or 5)-aminomethylglyoxaline and 4(or 5)-γ-aminopropylglyoxaline were required, but since the latter was not readily accessible its methyl homologue, 4(or 5)-γ-aminobutylglyoxaline, was prepared and tested in its place. Compared with 4(or 5)-β-aminoethylglyoxaline, the activity of these bases proved to be negligible.

4(or 5)-Aminomethylglyoxaline (I) has recently been described by Windaus and Opitz (*Ber.*, 1911, **44**, 1721), who prepared it by Curtius' method from glyoxaline-4(or 5)-acetic acid obtained from histidine. It may, however, readily be prepared synthetically by suitably oxidising 2-thiol-4(or 5)-aminomethylglyoxaline (II). It has previously been shown (this vol., p. 669) that the customary method of oxidising thiolglyoxalines to glyoxalines by means of nitric acid leads, in the case of this compound, to 4(or 5)-hydroxymethylglyoxaline (III). If, however, an oxidising agent not producing nitrous acid were employed, the formation of 4(or 5)-aminomethylglyoxaline would be possible. Other oxidising agents were therefore tried, and

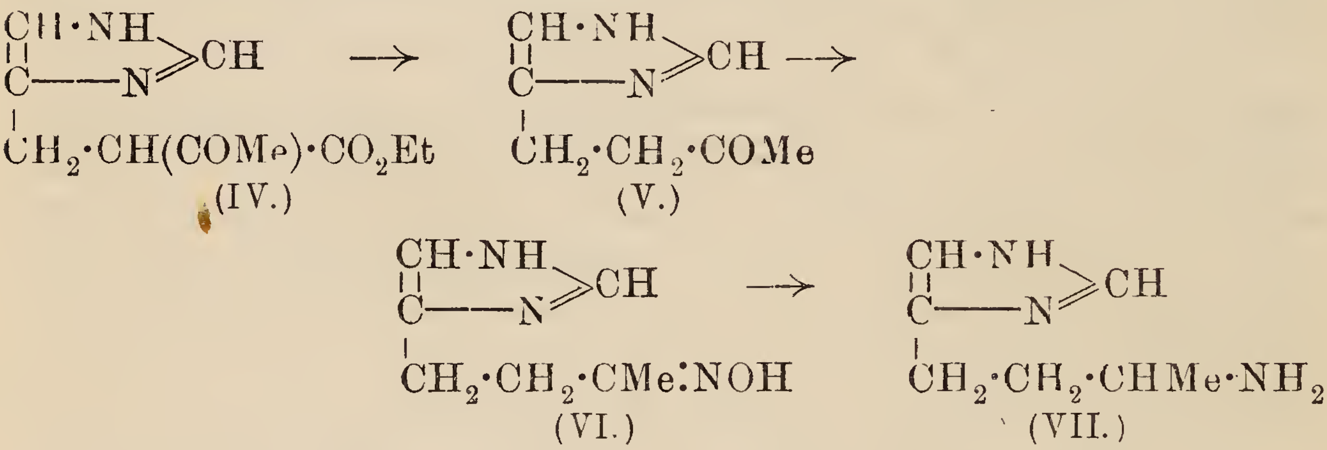


it was found that ferric chloride in calculated quantity oxidised 2-thiol-4(or 5)-aminomethylglyoxaline to 4(or 5)-aminomethylglyoxaline in a yield amounting to more than 50 per cent. of the theoretical:

Potassium permanganate is unsuitable for the oxidation of 2-thiol-4(or 5)-aminomethylglyoxaline to 4(or 5)-aminomethylglyoxaline, for it readily attacks the former substance, causing complete rupture of the glyoxaline ring; cold dilute aqueous solutions of potassium permanganate are immediately decolorised by 2-thiol-4(or 5)-aminomethylglyoxaline, but not by 4(or 5)-aminomethylglyoxaline or other glyoxalines not containing the 2-thiol group. This difference in behaviour is ascribed to the possibility of the thiol base reacting in the tautomeric thiocarbamide form as an unsaturated compound.

4(or 5)-γ-*Aminobutylglyoxaline* was readily prepared as follows:

Ethyl 4(or 5)-glyoxalinemethylacetoacetate (IV) (this vol., p. 1392) was converted into the corresponding ketone, 4(or 5)-γ-*ketobutylglyoxaline* (V), by hydrolysis with hydrochloric acid. This was next transformed into the oxime, 4(or 5)-γ-*oximinobutylglyoxaline* (VI), which on reduction by means of sodium amalgam and acetic acid gave 4(or 5)-γ-*aminobutylglyoxaline* (VII):



A quantity of αβ-bis[4(or 5)-glyoxaline]-propionitrile (VIII) (this vol., p. 677) which is formed as a by-product in the preparation of 4(or 5)-cyanomethylglyoxaline being available, it was thought of interest to reduce it to βγ-*bis*[4(or 5)-*glyoxaline*]-*propylamine* (IX), which may be regarded as an aminoethylglyoxaline containing a glyoxalinemethyl substituent. This reduction was carried out with sodium and alcohol, and the desired base was obtained, together with another compound, which was probably αβ-*bis*[4(or 5)-*glyoxaline*]-*propionic acid* (X):

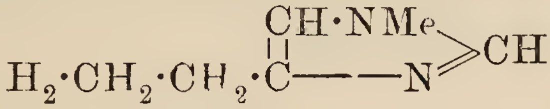
$$\underset{\text{(VIII.)}}{C_3H_3N_2\cdot CH_2\cdot CH(CN)\cdot C_3H_3N_2} \longrightarrow$$

$$\underset{\text{(IX.)}}{C_3H_3N_2\cdot CH_2\cdot CH(CH_2\cdot NH_2)\cdot C_3H_3N_2}, \text{ and}$$

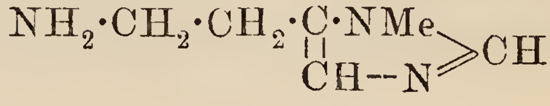
$$\underset{\text{(X.)}}{C_3H_3N_2\cdot CH_2\cdot CH(CO_2H)\cdot C_3H_3N_2}.$$

The physiological action of $\beta\gamma$-bis[4(or 5)-glyoxaline]-propylamine is very slight compared with that of 4(or 5)-β-aminoethylglyoxaline.

The two isomeric *N*-methyl derivatives of 4(or 5)-β-aminoethylglyoxaline in which the methyl group substitutes the imino-hydrogen atom of the glyoxaline ring were next prepared. These compounds, 1-methyl-4(and 5)-aminoethylglyoxaline (XI and XII),



(XI.)



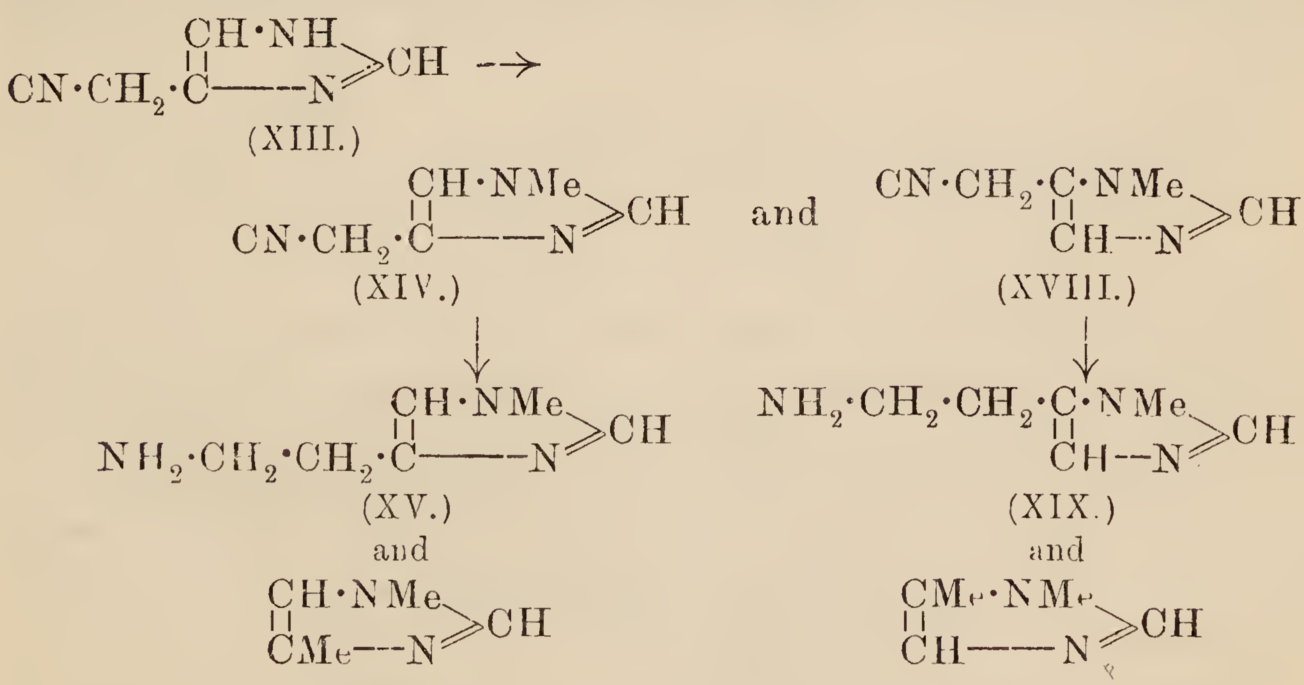
(XII.)

were obtained by reduction of the corresponding methylcyano-methylglyoxalines. Their physiological action is negligible compared with that of 4(or 5)-β-aminoethylglyoxaline.

4(or 5)-Cyanomethylglyoxaline (XIII) (this vol., p. 676) yields on methylation with methyl sulphate and alkali a mixture of the 1:4- and 1:5-methylcyanomethylglyoxalines, from which the former can readily be obtained in a pure state, and the latter less readily by fractional crystallisation of the picrates.

1-*Methyl*-4-*cyanomethylglyoxaline* (XIV) gave on reduction with sodium and alcohol 1-*methyl*-4-β-*aminoethylglyoxaline* (XV), together with small quantities of 1:4-dimethylglyoxaline (XVI) and 1-*methylglyoxaline*-4-*acetic acid* (XVII).

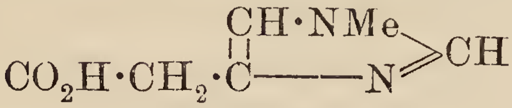
1-*Methyl*-5-*cyanomethylglyoxaline* (XVIII) when similarly treated yielded 1-*methyl*-5-β-*aminoethylglyoxaline* (XIX) and 1:5-dimethylglyoxaline (XX). As the constitution of the 1:4- and 1:5-dimethylglyoxalines has already been determined with a high degree of probability (Trans., 1910, **97**, 1814), orientation of the methylated cyanomethylglyoxalines and their other reduction products follows:



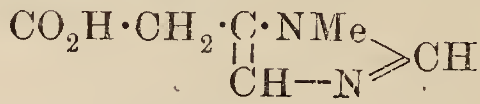
(XIII.) (XIV.) and (XVIII.) (XV.) and (XVI.) (XIX.) and (XX.)

1-Methylglyoxaline-4-acetic acid may readily be prepared by hydrolysing 1-methyl-4-cyanomethylglyoxaline with alkali. Its

ester, *ethyl 1-methylglyoxaline-4-acetate*, was prepared by the action of alcoholic hydrogen chloride on 1-methyl-4-cyanomethylglyoxaline:



(XVII.)



(XXI.)

1-*Methylglyoxaline-5-acetic acid* (XXI) was obtained by hydrolysing 1-methyl-5-cyanomethylglyoxaline with alkali.

Experimental.

Oxidation of 2-Thiol-4(or 5)-aminomethylglyoxaline to 4(or 5)-Aminomethylglyoxaline.

1·29 Grams of 2-thiol-4(or 5)-aminomethylglyoxaline (this vol., p. 672) were dissolved in 50 c.c. of water, added to a solution of 9·8 grams of ferric chloride in 100 c.c. of water, and the mixture digested for half an hour in the water-bath. Thirty c.c. of 10 per cent. aqueous sodium carbonate were then added, followed by a hot solution of 4·6 grams of picric acid in 100 c.c. of boiling water. The liquor was then boiled with a little animal charcoal and filtered, and on cooling 3·2 grams of pure 4(or 5)-aminomethylglyoxaline dipicrate separated in the first crop; this quantity represents 56 per cent. of the theoretical yield.

4(or 5)-Aminomethylglyoxaline dipicrate crystallises from water in hexagonal or diamond-shaped plates, which melt at 210—211° (corr.). It contains $1H_2O$, which is lost at 120°, but not at 100°. The water of crystallisation in this salt is not mentioned by Windaus and Opitz (*Ber.*, 1911, **44**, 1723), who give the melting point as 209°:

0·1749 * lost *nil* at 100°, lost 0·0054 at 120°. $H_2O = 3·1$.

0·2064 † gave 0·2550 CO_2 and 0·0496 H_2O. C = 33·7; H = 2·7.

$C_4H_7N_3,2C_6H_3O_7N_3,H_2O$ requires C = 33·5; H = 2·6; $H_2O = 3·1$ per cent.

4(or 5)-Aminomethylglyoxaline dihydrochloride was prepared by treating the picrate with hydrochloric acid, removing the picric acid by means of ether, evaporating the acid liquor to dryness, and crystallising the residue from water. It separates from water in colourless, prismatic needles, which contain $\frac{1}{2}H_2O$, and after drying at 100° melt at 244—245° (corr.) after sintering from about 235°. Its aqueous solution is strongly acid:

0·1262, air-dried salt, lost 0·0068 at 100°. $H_2O = 5·4$.

$C_4H_7N_3,2HCl,\frac{1}{2}H_2O$ requires $H_2O = 5·0$ per cent.

* Air-dried. † Dried at 100°.

For anhydrous salt: Found, C=28·0; H=5·6. Calc., C=28·2; H=5·3 per cent.

Windaus and Opitz (*loc. cit.*), who crystallised this salt from a mixture of methyl alcohol and ether, do not mention any water of crystallisation; they state that on heating, the salt sinters from 236° onwards.

4(or 5)-*Aminomethylglyoxaline hydrogen oxalate* crystallises from water in monoclinic, hexagonal plates, which decompose at 218° (corr.). It is anhydrous, and is sparingly soluble in cold water:

0·2478 gave 0·3158 CO_2 and 0·0898 H_2O. C=34·8; H=4·1.

$C_4H_7N_3,2C_2H_2O_4$ requires C=34·7; H=4·0 per cent.

4(or 5)-γ-*Ketobutylglyoxaline* [4(or 5)-*Glyoxaline-ethyl Methyl Ketone*], $CH_3·CO·CH_2·CH_2·C{\overset{\displaystyle CH·NH}{\Vert}}\!\!-\!\!-N \gg CH$.

Fifteen grams of ethyl 4(or 5)-glyoxalinemethylacetoacetate hydrogen oxalate (this vol., p. 1392) were converted into the base, and this boiled under a reflux condenser for three hours with 60 c.c. of hydrochloric acid and 90 c.c. of water. The liquid was then evaporated to dryness under diminished pressure, and the residue dissolved in a little water, mixed with sodium carbonate, and extracted with chloroform. The extract after drying and distillation of the solvent left the ketone as a viscid, brown oil, which solidified on keeping, forming large, buff crystals, melting at 76—78°, and amounting to 4·4 grams; this yield is 64 per cent. of the theoretical.

4(or 5)-γ-*Ketobutylglyoxaline* crystallises from anhydrous ethyl acetate in stout, colourless, prismatic needles, which melt at 80—81° (corr.). It is very readily soluble in water, alcohol, acetone, or chloroform, readily so in ethyl acetate, and very sparingly so in ether or benzene:

0·1278 gave 0·2854 CO_2 and 0·0882 H_2O. C=60·9; H=7·7.

$C_7H_{10}ON_2$ requires C=60·8; H=7·3 per cent.

The *picrate* crystallises from water or alcohol in fine, yellow needles, which melt at 192—193° (corr.). It is very sparingly soluble in cold water or alcohol, but fairly readily so in hot water:

0·1088 gave 0·1702 CO_2 and 0·0370 H_2O. C=42·6; H=3·8.

$C_7H_{10}ON_2,C_6H_3O_7N_3$ requires C=42·5; H=3·6 per cent.

4(or 5)-γ-*Oximinobutylglyoxaline*,

$$HO·N:CMe·CH_2·CH_2·C{\overset{\displaystyle CH·NH}{\Vert}}\!\!-\!\!-N \gg CH.$$

This oxime is readily prepared in good yield by heating on the water-bath an aqueous solution of the ketone with the calculated

amounts of hydroxylamine hydrochloride and sodium carbonate; on concentrating and cooling the solution, the oxime crystallises out, and is purified by recrystallisation from water.

4(or 5)-γ-*Oximinobutylglyoxaline* crystallises from water in clear, colourless plates, which melt at 152—153° (corr.). It is sparingly soluble in cold water or acetone, fairly readily so in alcohol or hot water, but very sparingly so in chloroform:

0·2134 gave 0·4284 CO_2 and 0·1407 H_2O. C=54·7; H=7·4.

$C_7H_{11}ON_3$ requires C=54·9; H=7·3 per cent.

The *picrate* crystallises from water in hard, spherical grains, which melt at 166—168° (corr.). This salt is sparingly soluble in cold, but readily so in hot, water.

4(or 5)-γ-*Aminobutylglyoxaline*,

$$CH_3{\cdot}CH(NH_2){\cdot}CH_2{\cdot}CH_2{\cdot}\underset{\displaystyle C\text{———}N}{\overset{\displaystyle CH{\cdot}NH}{\|}}\!\!>CH.$$

2·3 Grams of 4(or 5)-γ-oximinobutylglyoxaline were dissolved in 15 c.c. of alcohol and 5 c.c. of glacial acetic acid. Fifty grams of 3 per cent. sodium amalgam were then added, and the mixture well shaken and cooled with water. Enough water was supplied from time to time to dissolve the separated sodium acetate, and two further quantities, each of 5 c.c., of acetic acid and 50 grams of sodium amalgam were subsequently added. When the sodium amalgam had been used up, the liquor was diluted with about 100 c.c. of water, and poured into a hot solution of 7 grams of picric acid in 200 c.c. of water, when on cooling 4(or 5)-γ-aminobutylglyoxaline dipicrate crystallised out. After recrystallisation from water 4·1 grams of the pure salt were obtained, that is, 45 per cent. of the theoretical.

4(or 5)-γ-*Aminobutylglyoxaline dipicrate* crystallises from water in long, golden, somewhat serrated spikes, which melt at 247° (corr.) to a brown liquid, which then decomposes. This salt is anhydrous, and very sparingly soluble in cold, but fairly readily so in hot, water:

0·1163 gave 0·1638 CO_2 and 0·0350 H_2O. C=38·4; H=3·4.

$C_7H_{13}N_3,(C_6H_3O_7N_3)_2$ requires C=38·2; H=3·2 per cent.

Reduction of αβ-Bis[4(or 5)-*glyoxaline*]-*propionitrile.*

Nine grams of αβ-bis[4(or 5)-glyoxaline]-propionitrile hydrogen oxalate * were converted into the base in the manner previously described, and this was reduced by means of 5 grams of sodium

* This vol., p. 677; the formula of the base should read $C_9H_9N_5$.

and 75 c.c. of absolute alcohol. The reaction product was neutralised with hydrochloric acid, made strongly alkaline with sodium carbonate, evaporated to dryness under diminished pressure, and the residue completely extracted with absolute alcohol. After the removal of the bulk of the solvent, the extract was poured into a solution of 20 grams of picric acid in 500 c.c. of boiling water, when a viscous oil separated. After the solution had cooled somewhat it was decanted from the oil and filtered, when it deposited about 3 grams of crystals, melting at 195—200°. The very sparingly soluble oil also became crystalline on cooling, and was extracted with 500 c.c. of boiling water, filtered, and allowed to cool to about 50°, when 5·0 grams of orange needles, melting at 150—153°, separated; these were collected, and the mother liquor allowed to become quite cold, when a further 1·6 grams of crystals, melting at about 210°, separated.

The more sparingly soluble picrate was readily purified by crystallisation from water, and proved to be *βγ-bis*[4(or 5)-*glyoxaline*]-*propylamine tripicrate*; 3·4 grams of this salt were obtained in a pure state, decomposing at 158° (corr.), that is, 18 per cent. of the theoretical. The more easily soluble picrate was less readily purified; it melted and decomposed at 218—220° (corr.) when pure, and was probably *αβ-bis*[4(or 5)-*glyoxaline*]-*propionic acid dipicrate*:

0·1300, air-dried salt, lost 0·0072 at 100°. $H_2O = 5·5$.

$C_9H_{10}O_2N_4,(C_6H_3O_7N_3)_2,2H_2O$ requires $H_2O = 5·1$ per cent.

0·1010 * gave 0·1392 CO_2 and 0·0268 H_2O. C = 37·6; H = 3·0.

0·1232 * „ 0·1706 CO_2 „ 0·0331 H_2O. C = 37·8; H = 3·0.

$C_9H_{10}O_2N_4,(C_6H_3O_7N_3)_2$ requires C = 37·9; H = 2·4 per cent.

βγ-Bis[4(or 5)-*glyoxaline*]-*propylamine*,
$C_3H_3N_2\cdot CH_2\cdot CH(CH_2\cdot NH_2)\cdot C_3H_3N_2$.

The *tripicrate* crystallises from water in beautiful, orange-yellow, flat needles, which soften from 150° and decompose at 158° (corr.). This salt is sparingly soluble in hot, and very sparingly so in cold, water. It is anhydrous:

0·1330 gave 0·1786 CO_2 and 0·0330 H_2O. C = 36·6; H = 2·8.

$C_9H_{13}N_5,(C_6H_3O_7N_3)_3$ requires C = 36·9; H = 2·5 per cent.

The *trihydrochloride* was prepared by treating the picrate with hydrochloric acid and ether, and after evaporation of the excess of acid was obtained as a colourless varnish. This readily became crystalline when warmed with alcohol. The crystals were collected, dissolved in very little water, and hot alcohol added to the solution,

* Dried at 100°.

when the salt separated in beautiful, colourless, refracting prisms. The air-dried salt contains a molecule of water of crystallisation, which is not lost at 100°, but probably escapes at about 140°, for on heating the salt sinters at this temperature, but then remains unchanged until it melts at 235—237° (corr.). It is readily soluble in water, giving an acid solution, but is insoluble in absolute alcohol:

0·1382 gave 0·1730 CO_2 and 0·0730 H_2O. C = 34·1; H = 5·9.

0 1482 „ 0·1981 AgCl. Cl = 33·1.

$C_9H_{13}N_5,3HCl,H_2O$ requires C = 33·9; H = 5·7; Cl = 33·4 per cent.

Methylation of 4(or 5)-*Cyanomethylglyoxaline.*

Twenty grams of 4(or 5)-cyanomethylglyoxaline (this vol., p. 676) were dissolved in 80 c.c. of 10 per cent. aqueous sodium hydroxide, and shaken with 16 grams of methyl sulphate added gradually while the liquid was shaken and cooled by running water. Another 70 c.c. of 10 per cent. aqueous sodium hydroxide and 16 grams of methyl sulphate were then added. The clear brown liquor was completely extracted by chloroform, and the solvent removed from the extract, when a brown oil resulted. This was dissolved in water, and poured into 2100 c.c. of warm 2 per cent. picric acid solution, when most of the 1-*methyl*-4-*cyanomethylglyoxaline picrate* crystallised out at once in a pure state. On concentrating the mother liquors, 1-*methyl*-5-*cyanomethylglyoxaline picrate* separated out, mixed with small quantities of its isomeride, and it was purified by recrystallisation from water.

There were isolated 28·5 grams of 1-methyl-4-cyanomethylglyoxaline picrate, melting at 209—210° (corr.), and 9·9 grams of 1-methyl-5-cyanomethylglyoxaline picrate, melting at 156—157° (corr.), these quantities amounting to 43 and 15 per cent. of the theoretical respectively.

1-*Methyl*-4-*cyanomethylglyoxaline*, $\begin{array}{l} \qquad\qquad\;\; CH\cdot NMe \\ \qquad\qquad\;\; \| \\ CN\cdot CH_2\cdot C\text{———}N \end{array}\!\!>\!CH.$

This base crystallises from chloroform in clusters of plates, which melt at 34—36° (corr.). It is very deliquescent, and readily soluble in water and the usual organic solvents, with the exception of ether and light petroleum:

0·1337 * gave 0·2917 CO_2 and 0·0731 H_2O. C = 59·5; H = 6·1.

$C_6H_7N_3$ requires C = 59·5; H = 5·8 per cent.

The *hydrogen oxalate* crystallises from water or alcohol in

* Dried at 100°.

prismatic needles, which melt at 116—117° (corr.). It is readily soluble in water, but sparingly so in alcohol:

0·1503 gave 0·2496 CO_2 and 0·0572 H_2O. C=45·3; H=4·3.
0·1143 „ 19·6 c.c. N_2 at 18° and 759 mm. N=20·2.
$C_6H_7N_3,C_2H_2O_4$ requires C=45·5; H=4·3; N=19·9 per cent.

The *picrate* crystallises from water in flat, fern-like clusters of stout needles, or in rods of a rather pale yellow colour, which melt at 209—210° (corr.). It is anhydrous, and is very sparingly soluble in cold, but fairly readily so in hot, water:

0·1530 gave 0·2290 CO_2 and 0·0395 H_2O. C=40·8; H=3·0.
$C_6H_7N_3,C_6H_3O_7N_3$ requires C=41·1; H=2·9 per cent.

The *mercurichloride* and *mercuri-iodide* both readily crystallise from water in long needles.

1-*Methyl*-5-*cyanomethylglyoxaline*, $\begin{matrix} CN\cdot CH_2\cdot C\cdot NMe \\ \| \\ CH\text{—}N \end{matrix}\!\!>\!CH.$

This base was obtained as an oil, which did not crystallise when kept for several hours at 0°. It is readily soluble in water, alcohol, or chloroform.

The *hydrogen oxalate* crystallises from alcohol in prisms, which sinter slightly from 135°, and melt and effervesce at 139—140° (corr.). It is anhydrous. It is readily soluble in water, but sparingly so in alcohol:

0·1580 gave 0·2632 CO_2 and 0·0612 H_2O. C=45·4; H=4·3.
$C_6H_7N_3,C_2H_2O_4$ requires C=45·5; H=4·3 per cent.

The *picrate* crystallises from water in large, pale yellow, glistening leaflets, which melt at 156—157° (corr.). This salt is anhydrous, sparingly soluble in cold, but readily so in hot, water:

0·1507 gave 0·2284 CO_2 and 0·0411 H_2O. C=41·3; H=3·1.
$C_6H_7N_3,C_6H_3O_7N_3$ requires C=41·1; H=2·9 per cent.

1-*Methylglyoxaline*-4-*acetic Acid*, $\begin{matrix} CH\cdot NMe \\ \| \\ CO_2\cdot H\cdot CH_2\cdot C\text{———}N \end{matrix}\!\!>\!CH.$

0·75 Gram of 1-methyl-4-cyanomethylglyoxaline was dissolved in 20 c.c. of water, and boiled with 10 c.c. of 10 per cent. aqueous sodium hydroxide until no more ammonia was evolved. Then 9 c.c. of 10 per cent. hydrochloric acid were added, followed by 1·5 grams of picric acid in 40 c.c. of boiling water. On cooling, 1·5 grams of 1-*methylglyoxaline*-4-*acetic acid picrate* separated in large, striated prisms, melting at 187—189° (corr.), and a further 0·4 gram equally pure was obtained on concentrating the mother liquor, the yield thus amounting to 83 per cent. of the theoretical:

0·1209 gave 0·1751 CO_2 and 0·0332 H_2O. C = 39·5; H = 3·1.

$C_6H_8O_2N_2,C_6H_3O_7N_3$ requires C = 39·0; H = 3·0 per cent.

Ethyl 1-*Methylglyoxaline*-4-*acetate*, $C_4H_5N_2 \cdot CH_2 \cdot CO_2Et$.

Eight grams of 1-methyl-4-cyanomethylglyoxaline picrate were converted into the base, and this boiled for two hours with 50 c.c. of 15 per cent. absolute alcoholic hydrogen chloride, when ammonium chloride separated. The mixture was evaporated to dryness under diminished pressure, dissolved in water, mixed with sodium carbonate, and extracted with chloroform, when ethyl 1-methylglyoxaline-4-acetate was obtained as a brown oil. This was converted into the picrate, and purified by crystallisation from water, when 4·2 grams of the pure salt were obtained, that is, 46 per cent. of the theoretical.

Ethyl 1-*methylglyoxaline*-4-*acetate picrate* crystallises from water in long, yellow fibres, having the appearance of glass wool. It is very sparingly soluble in cold, but readily so in hot, water. It melts at 133—134° (corr.):

0·1092 * gave 0·1700 CO_2 and 0·0370 H_2O. C = 42·4; H = 3·8.

$C_8H_{12}O_2N_2,C_6H_3O_7N_3$ requires C = 42·3; H = 3·8 per cent.

1-*Methylglyoxaline*-5-*acetic Acid*, $\begin{array}{l} CO_2H \cdot CH_2 \cdot C \cdot NMe \\ \qquad\qquad\quad \| \\ \qquad\qquad\quad CH{-}{-}N \end{array} \!\!> CH.$

This compound was prepared by hydrolysis of its nitrile, and isolated as the *picrate*. This salt crystallises from water in beautiful, hexagonal plates, which melt at 180—181° (corr.), after sintering a few degrees earlier. It is anhydrous and sparingly soluble in cold, but readily so in hot, water:

0·1200 gave 0·1732 CO_2 and 0·0358 H_2O. C = 39·4; H = 3·3.

$C_6H_8O_2N_2,C_6H_3O_7N_3$ requires C = 39·0; H = 3·0 per cent.

Reduction of 1-*Methyl*-4-*cyanomethylglyoxaline*.

Seven grams of 1-methyl-4-cyanomethylglyoxaline were reduced by means of 10 grams of sodium and 100 c.c. of absolute alcohol. The reaction product was acidified with hydrochloric acid, made strongly alkaline with sodium carbonate, evaporated to dryness under diminished pressure, and the residue extracted with alcohol. The alcoholic extract was evaporated to dryness, and the residue extracted successively with ether, ethyl acetate, and absolute alcohol.

The ethereal extract amounted to 3·0 grams; it was dissolved

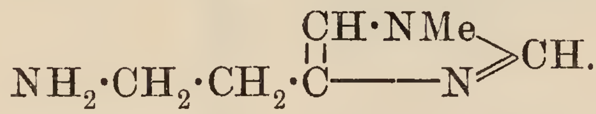
* Dried at 100°.

in water, and poured into a litre of warm 1 per cent. aqueous picric acid, when 6·6 grams of 1-*methyl*-4-β-*aminoethylglyoxaline dipicrate* separated in a pure state on cooling. The mother liquor was extracted with ether to remove free picric acid and evaporated to low bulk, when about 0·5 gram of a crude picrate, melting at about 140°, separated. After several crystallisations from water, a very small amount of 1 : 4-dimethylglyoxaline picrate was isolated from it, but was not obtained quite pure. This salt melted at 162—163° (corr.), the pure salt (Trans., 1910, **97**, 1819) melting at 167—168° (corr.) in the same bath, whilst a mixture of the two melted at 162—163° (corr.), and a mixture of this salt with 1 : 5-dimethylglyoxaline picrate at 135—140°.

The ethyl acetate extract afforded a further 1·3 grams of pure 1-methyl-4-β-aminoethylglyoxaline dipicrate, so that the total yield of this compound amounted to 7·9 grams, that is, 23 per cent. of the theoretical.

The absolute alcohol extract gave, with picric acid, at first an amorphous precipitate, but later a small quantity of 1-methylglyoxaline-4-acetic acid picrate.

1-*Methyl*-4-β-*aminoethylglyoxaline*,



The *dipicrate* crystallises from water in large, flat needles, which melt at 217° (corr.). It is very sparingly soluble in cold water, and is anhydrous:

0·1803 gave 0·2468 CO_2 and 0·0498 H_2O. C = 37·3; H = 3·1.

$C_6H_{11}N_3,(C_6H_3O_7N_3)_2$ requires C = 37·0; H = 2·9 per cent.

The *dihydrochloride* was prepared from the dipicrate by means of hydrochloric acid and ether. It crystallises from absolute alcohol in colourless prisms, which melt at 204—206° (corr.), after drying at 100°. It is deliquescent, and readily soluble in water, but sparingly so in absolute alcohol:

0·1186 * gave 0·1596 CO_2 and 0·0708 H_2O. C = 36·7; H = 6·7.

$C_6H_{11}N_3,2HCl$ requires C = 36·4; H = 6·6 per cent.

Reduction of 1-*Methyl*-5-*cyanomethylglyoxaline. Formation of* 1-*Methyl*-5-β-*aminoethylglyoxaline.*

Three grams of 1-methyl-5-cyanomethylglyoxaline were reduced by means of sodium and alcohol, and the products worked up as in the case of the 1 : 4-compound.

The combined ethereal and ethyl acetate extracts gave first an amorphous picrate, then small quantities of 1-*methyl*-5-β-*amino*-

ethylglyoxaline dipicrate, which formed yellow needles, melting at 201° (corr.), after drying at 100°:

0·1181 * gave 0·1615 CO_2 and 0·0305 H_2O. C=37·3; H=2·9.

$C_6H_{11}N_3,(C_6H_3O_7N_3)_2$ requires C=37·0; H=2·9 per cent.

The mother liquor from this salt then gave a small quantity of 1 : 5-dimethylglyoxaline picrate in clusters of slender needles, melting at 167—168° (corr.):

0·0907 gave 0·1345 CO_2 and 0·0267 H_2O. C=40·4; H=3·3.

$C_5H_8N_2,C_6H_3O_7N_3$ requires C=40·6; H=3·4 per cent.

This salt was identified by determination of the melting points of its mixtures with pure 1 : 4- and 1 : 5-dimethylglyoxaline picrates (Trans., 1910, 97, 1819), when it was found that the mixture with the 1 : 4-salt melted at 135—140°, whilst that with the 1 : 5-salt still melted at 167—168° (corr.).

The alcoholic extract gave a very small quantity of a crystalline picrate which melted at 162—175°; it was probably impure 1-methylglyoxaline-5-acetic acid picrate, but the quantity obtained was insufficient for identification.

The Wellcome Chemical Works,
Dartford, Kent.

* Dried at 100°.

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